Amendments to the Specification

Please replace the paragraph at page 13, lines 22-30 with the following amended paragraph:

Figure 24 is a graph illustrating the effect of anti-CD9 antibody ~~antidody~~ mAb7 on SMC migration. Cultured human coronary SMC migration was measured via a monolayer wounding assay as described in material and methods. After scratch, the cells were culture in 2% serum and treated for 24 hours without or with 1, 10 and 100 μg/ml mAb7. Group treated with 100 μg/ml normal mouse IgG as non-specific protein treatment control. Serum free media group as negative control. Cell migration was expressed as the distance migrated in the 24 hours. Results are the mean $\pm$ SEM of 6 experiments. *$p<0.05$, ** $p< 0.01$ and *** $p<0.001$ vs the 2% serum group without antibody.

Please replace the paragraph at page 14, lines 16-26 with the following amended paragraph:

Figures 27A-E illustrate the immunostaining of CD9 in mouse normal and ligation injured carotid arteries. Figure 27A is an image of CD9 ~~immumostaining~~ immunostaining with hematoxylin counterstaining in normal uninjured artery; Figure 27B is an image of double ~~immumostaining~~ immunostaining with anti-CD9 and anti-α-smooth muscle actin monoclonal antibody in normal uninjured artery; Figure 27C is an image of CD9 ~~immumostaining~~ immunostaining with hematoxylin counterstaining in injured artery; Figure 27D is an image of injured carotid arteries immunostained with negative control antibodies; Figure ~~27D~~ 27E is an image of double ~~immumostaining~~ immunostaining with anti-CD9 and anti-α-smooth muscle actin monoclonal antibody in injured artery; and Figure ~~27E~~ 27F is an image of double ~~immumostaining~~ immunostaining with anti-CD9 and anti-PCNA monoclonal antibody in injured artery. CD9 positive staining is in brown, while α-smooth muscle actin and PCNA positive staining is gray/black.

Please amend the paragraph at page 20, lines 27-31 with the following amended paragraph:

Preferred antibodies are those that bind to preferred CD9 polypeptides or peptides of the present invention or to α5 integrin. One exemplary antibody is the monoclonal antibody

mAb7, which is believed to recognize the peptide PKKDV (SEQ ID NO: 3). Another exemplary antibody is the polyclonal antibody PB1, which recognizes ~~recoginizes~~ α5 integrin.

Please amend the paragraph at page 21, line 31 to page 22, line 19, with the following amended paragraph:

A similar aspect of the present invention relates to a method of modifying adhesion, motility, or spreading of a CD9-expressing cell on fibronectin. To achieve the modified phenotypes, CD9 expression levels or CD9 activity on CD9-expressing cells can be modified. As noted above, enhanced CD9 expression levels inhibit adhesion of the CD9-expressing cell and enhance motility and spreading of the CD9-expressing cell, and inhibited CD9 activity enhances adhesion of the CD9-expressing cell and inhibits motility and spreading of the CD9-expressing cell. Enhanced or reduced CD9 expression ~~expresseion~~ levels can be achieved by gene therapy approaches described hereinafter whereas changes in CD9 activity can be achieved either by (i) contacting CD9 EC2 domains on a cell with an agent that binds to the CD9 EC2 domains, or (ii) contacting fibronectin with one or more polypeptide fragments of CD9 that include at least a part of a fibronectin-binding domain. Both approaches can be carried out simultaneously or in succession. Regardless of the approach, the various options modify adhesion, spreading, or motility of a CD9-expressing cell on fibronectin. Suitable agents that can be employed to interfere with CD9 binding to fibronectin include, without limitation, antibodies or fragments that bind to CD9 (or domains thereof) as described above and peptidomimetic small molecules identified according to the screening procedures as described in the Examples *infra*. In a preferred embodiment of the invention, antibodies or fragments of the present invention can be used in relation to the first approach, whereas CD9 peptides or polypeptides of the present invention can be used in relation to the second approach.

Please amend the paragraph at page 26, lines 17-29 with the following amended paragraph:

In general, construction of a transgene involves inserting a DNA coding sequence into an expression vector for subsequent introduction into cells that are to be transformed. The expression vector contains appropriate promoter and 3' polyadenylation signals to drive *in vivo* transgene expression in mammalian (preferably human) hosts. Promoters of varying strength

can be employed depending on the degree of expression desired. One of skill in the art can readily select appropriate promoters based on their ~~their~~ strength as a promoter. Alternatively, an inducible promoter can be employed for purposes of controlling when expression of the transgene occurs. One of skill in the art can readily select appropriate inducible promoters from those known in the art. Finally, tissue specific promoters can be selected to restrict the efficacy of any transgene to a particular tissue or a particular cell-type within a tissue. Tissue specific promoters are known in the art and can be selected based upon the tissue or cell type to be treated.

Please amend the paragraph at page 48, line 16, to page 49, line 2, with the following amended paragraph:

Human SMC CD9 expression was determined by flow cytometry and immunofluoresencent microscopy analysis. Flow cytometry analysis were performed utilizing an indirect labeling method as described in the Materials & Methods for Examples 8-13. Briefly, serum free arrested SMC and 5% serum stimulated SMC were collected, washed with DMEM medium by centrifugation at 800g for 5 minutes. Cells were resuspended at a concentration of 10^6/ml in labeling medium. 5×10^6cells in labeling medium were labeled for CD9 expression with 4 μg mAb7 monoclonal antibody or a specific mouse control IgG and incubated for 30 minutes at 4 °C, followed by centrifugation for 5 minutes at 2200g. The supernatants were removed and the cell pellets resuspended in 100μl of labeling medium. Secondary antibody, 5μg of goat anti-mouse IgG-FITC was added and incubated at 4°C for 30 minutes. Samples were centrifuged, resuspended in 1 ml of labeling medium, and analyzed for bound flurescein on Becton Dickinson FACSCCalibur Flow Cytomemter using CellQuest data analysis software. For Immunofluoresencent Microscopy Analysis, cells were incubated with Mab7 for 30 minutes at 4 °C. After washing, bound mAb was detected by incubation with 5μg/ml Alexa Fluor 488-conjugated goat anti-mouse antibody for another 30 minutes at 4 °C. Finally, cells were washed, fixed for 15 minutes with 4% paraformaldehyde, and ~~converslips~~ coverslips were ~~appied~~ applied with Fluoromount-G. The stained cells were examined using a Zeiss LSM 510 immunofluoresencent microscopy system.

Please amend the paragraph at page 53, lines 14-31, with the following amended paragraph:

The CD9-CHO-N3 clonal cell line was isolated from CHO cells transfected with PRvCMVCD9 (Lanza et al., *J. Biol. Chem.* 266:10638-10645 (1991), which is hereby incorporated by reference in its entirety). Polycarbonate filters coated with either fibrinogen or BSA had no adhered CD9-CHO-N3 cells in motility assays after 6 hours. CD9-CHO-A6 clone described in this study was derived from CHO cells transfected with PRvCMVCD9-A6. Both CD9-CHO-N3 and CD9-CHO-A6 cell clones had high surface expression of CD9 as demonstrated by flow cytometry. For example, over 93% of CD9-CHO-A6 cells expressed CD9 with a mean ~~fluoresence~~ fluorescence intensity (MFI) of 760 on labeling with mAb7 compared with Mock-CHO cells with an MFI of 6.7. To demonstrate that CD9 effects on CHO cell motility were not due to aberrant clones, two clonally heterogenous populations of CD9-expressing CHO cells were generated. Both CD9-CHO-H1 and CD9-CHO-H2 had equivalent CD9 cell surface density seen with clones CD9-CHO-A6 and CD9-CHO-N3. Additionally, a heterogenous CD9-expressing CHO cell population was produced using the pREP4CD9 expression vector. CD9-CHO-REP4 expressed CD9 with an MFI of 46, demonstrating that CD9-CHO-REP4 cells expressed significantly less CD9 than the clonal or heterogenous CD9-expressing CHO cells transfected with the PRvCMVCD9 expression construct.

Please amend the paragraph at page 63, line 20, to page 64, line 2, with the following amended paragraph:

To further investigate the effect of CD9 expression on adhesive cell functions, the localization of proteins typically incorporated into adhesion complexes was examined. In the CHO cell, the integrin $\alpha_5\beta_1$ is predominately responsible for cell-matrix and membrane-cytoskeleton interaction (Woods et al., *EMBO J.* 5:665-670 (1986); Humphries, *J. Cell Sci.* 97:585-592 (1990); Ruoslahti E., *J. Clin. Invest.* 87:1-5 (1991), each of which is hereby incorporated by reference in its entirety ~~entiretey~~). As previously described, (Nakamura et al., *J. Biol. Chem.* 275:18284-19290 (2000), which is hereby incorporated by reference in its entirety ~~entiretey~~) flow cytometric analysis of MOCK-, CD9-, and mutant CHO cells shows transfection of CD9 cDNA did not alter the surface expression of integrin $\alpha_5\beta_1$. Laser scanning confocal microscopy images confirmed the equivalent staining (Figure 12) of $\alpha_5\beta_1$ on these clones.

Equivalent amounts of F-actin also appeared to be present in these cells. However, CD9 expression reduced $\alpha_5\beta_1$ colocalization with F-actin (see merge). CHO Δ133-192 cells expressing a truncated EC2 had equivalent colocalization of $\alpha_5\beta_1$/F-actin, as seen in MOCK CHO cells. These data suggest that CD9 EC2 down-regulates $\alpha_5\beta_1$/F-actin interactions.

Please amend the paragraph at page 64, lines 3-9, with the following amended paragraph:

An important signaling molecule typically found in focal adhesion complexes is FAK (Cary et al., *Front Biosci.* 4:D102-D113 (1999), which is hereby incorporated by reference in its entirety ~~entiretey~~). Immunolabeled FAK and F-actin of basal images of MOCK, A6, and Δ133-192 cells grown on FN showed that CHO A6 cells had significantly less FAK staining (Figure 13) compared with CHO MOCK or CHO Δ133-192 cells. In addition, a reduction in FAK colocalization with F-actin was also observed in CHO A6 cells compared to CHO MOCK and CHO Δ133-192 cells.

Please amend the paragraph at page 76, lines 7-17 with the following amended paragraph:

As shown in Figure 27A, in normal non-injured arteries, CD9 was expressed in endothelial cells and in the cells at media and adventitia. In order to determine whether CD9 is expressed in vascular SMCs, double immunostaining ~~immumostaining~~ with anti-CD9 and anti-α-smooth muscle actin monoclonal antibody was performed. As shown in Figure 27B, CD9 was expressed in SMCs. In vessels after two weeks of injury, the expression ~~expressed~~ of CD9 was increased (Figure 27C). Not only the medial SMCs had positive staining, but there was also strong CD9 positive staining in SMCs at neointima (Figure 27E ~~27D~~). To test the CD9 expression change in proliferating cells, double immunostaining ~~immumostaining~~ with anti-CD9 and anti-PCNA (a biomarker for proliferating cells) monoclonal antibody was used. As shown in Figure 27F ~~27E~~, there was stronger positive staining in proliferating cells than that in non-proliferating cells. Control staining with negative antibody is shown in Figure 27D.

Please amend the paragraph at page 76, line 35, to page 77, line 12, with the following amended paragraph:

CD9 is a major cell surface protein, which was first identified on lymphohematopoietic cells (Boucheix et al., *J. Biol. Chem.* 266:117-122 (1991), which is hereby incorporated by reference in its entirety ~~entirett~~). It was demonstrated that CD9 is expressed in cultured human coronary SMCs *in vitro* and in normal uninjured mouse vascular SMSc *in vivo*. In proliferating SMCs, CD9 expression is increased. The results are similar to that from recent reports (Lijnen et al. *Thromb. Haemost.* 83:956-961 (2000); Nishida et al. *Arterioscler. Thromb. Vasc. Biol.* 20:1236-1243 (2000); Scherberich et al. *Arterioscler. Thromb. Vasc. Biol.* 18:1691-1697 (1998); Le Naour et al., *Science* 287:319-321 (2000), each of which is hereby incorporated by reference in its entirety). It was also demonstrated, for the first time, that CD9 expression is increased in vessels after ligation injury. The high expression in SMCs and expression change in different phenotype SMCs suggested that CD9 likely plays important roles in SMC functions such as migration, proliferation, and the response to injury.